



| | |
|--------------------|--|
| Title | Blocking the PI3K/AKT pathway can impair metastasis of esophageal cancer |
| Author(s) | Xu, W; Li, B; Li, YY; Tsao, SW; Cheung, ALM |
| Citation | The 2014 World Cancer Congress (WCC), Melbourne, Australia, 3-6 December 2014, abstract 942 |
| Issued Date | 2014 |
| URL | http://hdl.handle.net/10722/207780 |
| Rights | Creative Commons: Attribution 3.0 Hong Kong License |

BLOCKING THE PI3K/AKT PATHWAY CAN IMPAIR METASTASIS OF ESOPHAGEAL CANCER (no. 942)

Wen Wen Xu, Bin Li, Yuk Yin Li, Sai Wah Tsao, Annie L.M. Cheung The University of Hong Kong, Hong Kong

BACKGROUND: Esophageal cancer (EC) is an aggressive malignancy with increasing incidence and poor outcome (1). New therapeutic strategies are urgently required. The phosphatidylinositol 3-kinase (PI3K)/AKT signal pathway has been documented as a central hub for the malignant behaviors of cancer cells (2). However, the functional role and therapeutic effect of PI3K/AKT inhibitors in esophageal cancer metastasis is underappreciated. **AIM:** We aim to study the clinical significance of PI3K/AKT signaling pathway in EC metastasis and evaluate the therapeutic effect of PI3K/AKT-targeted therapy. **METHODS:** A highly invasive cancer cell line (KYSE410-I3) was established by serial selection of the EC cells invading through the matrigel-coated Boyden chamber. Cell migration and invasion were determined using Boyden chamber migration and invasion assays. Western blot and immunohistochemistry were used to detect protein expressions in cell lysates and in a tissue microarray containing 40 pairs of primary/metastatic EC respectively. The experimental metastasis mouse model was established by intravenously injection of EC cells via the tail vein. **RESULTS:** We found elevated expression of phosphorylated-AKT (p-AKT) in the invasive EC cells compared with parental cells. Moreover, increased p-AKT expression was found in metastatic tumors compared with matched primary tumors. Overexpression of phosphatase and tensin homolog (PTEN), or treatment with PI3K specific inhibitors (LY294002 and Wortmannin), significantly suppressed EC cell migration and invasion, suggesting a functional role for PI3K/AKT in metastasis. Inhibition of the PI3K pathway also significantly decreased N-cadherin and increased E-cadherin expressions. The results from bioluminescent imaging, histological and western blot analyses collectively showed that Wortmannin significantly impaired lung metastasis in mice without obvious toxic effects. **CONCLUSIONS:** PI3K/AKT signaling pathway is constitutively activated in esophageal metastatic tumor tissues and may be a valid therapeutic target for metastatic esophageal cancer.

1. Ferlay,J., Shin,H.R., Bray,F., Forman,D., Mathers,C., and Parkin,D.M. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int. J. Cancer* 127, 2893-2917.
2. Vivanco,I. and Sawyers,C.L. (2002). The phosphatidylinositol 3-Kinase AKT pathway in human cancer. *Nat. Rev. Cancer* 2, 489-501.
3. Vivanco,I. and Sawyers,C.L. (2002). The phosphatidylinositol 3-Kinase AKT pathway in human cancer. *Nat. Rev. Cancer* 2, 489-501.